

CLAIMS

1. A single-chain Fv (sFv) polypeptide defining a binding site which exhibits the immunological binding properties of an immunoglobulin molecule which binds c-erbB-2 or a c-erbB-2-related tumor antigen, said sFv comprising at least two polypeptide domains connected by a polypeptide linker spanning the distance between the C-terminus of one domain and the N-terminus of the other, the amino acid sequence of each of said polypeptide domains comprising a set of complementarity determining regions (CDRs) interposed between a set of framework regions (FRs), said CDRs conferring immunological binding to said c-erbB-2 or c-erbB-2-related tumor antigen.

2. The single-chain Fv polypeptide of claim 1 wherein said CDRs are substantially homologous with the CDRs of the c-erbB-2-binding immunoglobulin molecules selected from the group consisting of 520C9, 741F8, and 454C11 monoclonal antibodies.

3. The single-chain Fv polypeptide of claim 2 wherein the amino acid sequence of each of said sFv CDRs and each of said FRs are substantially homologous with the amino acid sequence of CDRs and FRs of the variable region of 520C9 antibody.

4. The single-chain Fv polypeptide of claim 1 wherein said polypeptide linker comprises the amino acid sequence as set forth in the Sequence Listing as amino acid residue numbers 118 through 133 in SEQ ID NO:4.

5. The single-chain Fv polypeptide of claim 1 wherein said polypeptide linker comprises an amino acid sequence selected from the group of sequences set forth as amino acid residues 116-135 in SEQ ID NO:6, or 122-135 in SEQ. ID NO:15 and the amino acid sequences set forth in SEQ ID NO: 12 and SEQ ID NO: 14.

6. The single-chain Fv polypeptide of claim 1 further comprising a remotely detectable moiety bound thereto to permit imaging of a cell bearing said c-erbB-2-related tumor antigen.

7. The single-chain Fv polypeptide of claim 6 wherein said remotely detectable moiety comprises a radioactive atom.

8. The single-chain Fv polypeptide of claim 1 further comprising, linked to the N or C terminus of said linked domains, a third polypeptide domain comprising an amino acid sequence defining CDRs interposed between FRs and defining a second immunologically active site.

9. The single-chain Fv polypeptide of claim 8, further comprising a fourth polypeptide domain, wherein said third and fourth polypeptide domains together comprise a second site which immunologically binds a c-erbB-2-related tumor antigen.

10. The single-chain Fv polypeptide of claim 1 or 7 further comprising a toxin linked to the N or C terminus of said linked domain.

11. The single-chain Fv polypeptide of claim 10 wherein said toxin comprises a toxic portion selected from the group: Pseudomonas exotoxin, ricin, ricin A chain, phytolectin and diphtheria toxin.

12. The single-chain Fv polypeptide of claim 10 wherein said toxin comprises at least a portion of the ricin A chain.

13. A DNA sequence encoding the polypeptide chain of claim 1.

14. A method of producing a single chain polypeptide having specificity for a c-erbB-2-related tumor antigen, said method comprising the steps of:

(a) transfecting the DNA of claim 13 into a host cell to produce a transformant; and

(b) culturing said transformant to produce said single-chain polypeptide.

15. A method of imaging a tumor expressing a c-erbB-2-related antigen, said method comprising the steps of:

(a) providing an imaging agent comprising the polypeptide of claim 7;

(b) administering to a mammal harboring said tumor an amount of said imaging agent together with a physiologically-acceptable carrier sufficient to permit extracorporeal detection of said tumor after allowing said agent to bind to said tumor; and

(c) detecting the location of said remotely detectable moiety in said subject to obtain an image of said tumor.

16. A host cell transfected with a DNA of claim 13.

17. A method of inhibiting in vivo growth of a tumor expressing a c-erbB-2-related antigen, said method comprising:

administering to a patient harboring the tumor a tumor inhibiting amount of a therapeutic agent comprising a single-chain Fv of claim 1 and at least a first moiety peptide bonded thereto, said first moiety having the ability to limit the proliferation of a tumor cell.

18. The method of claim 17 wherein said first moiety comprises a cell toxin or a toxic fragment thereof.

19. The method of claim 17 wherein said first moiety comprises a radioisotope sufficiently radioactive to inhibit proliferation of said tumor cell.

20. A DNA sequence encoding the polypeptide chain of claim 10.